2.





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Patent Claims

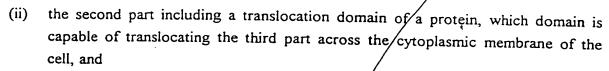
Method of treating a patient with a disorder, characterized by an activating mutation in the Ras proto-oncogene, comprising contacting cells of said patient with a protein having the toxic activity of Clostridium sordellii toxin LT under conditions favoring inactivating of Ras by glucosylation of Ras subfamily proteins.

- The method according to claim 1, characterized in that the disorder is pancreas or colon cancer.
- 3. The method according to claim 1 wherein said protein is an immunotoxin.
- 4. The method according to claims 1 to 3 wherein said immunotoxin contains a first part, a second part, and a third part, connected by covalent bonds:
 - (i) the first part including a target cell specific binding domain, which domain is able to cause the immunotoxin to bind to said patient's cell;
 - (ii) the second part including a translocation domain of a protein, which domain is capable of translocating the third part across the cytoplasmic membrane of the cell, and
 - (iii) the third part including a polypeptide with the toxic activity of the catalytic domain of toxin LT from Clostridium sordellii LT.
- 5. The method according to claims 4, characterized in that the target cell specific binding domain is an antibody of an active fragment thereof.
- 6. The method according to claim 5 wherein the antibody or active fragment thereof specifically binds to tumor cells.

A composition useful in treating a pathological condition, characterized by activation of Ras proto-oncoproteins, comprising a first part, a second part, and a third part, connected by covalent bonds.

(i) the first part including a target cell specific binding domain, which domain is able to cause the immunotoxin to bind to said patient's cell;





(iii) the third part including a polypeptide with the toxic activity of the catalytic domain of toxin LT from Clostridium sordellii LT,

and a pharmaceutically acceptable carrier.

- An immunotoxin which contains a first part, a second part, and a third part, connected by covalent bonds:
 - (i) the first part including a target cell specific binding domain, which domain is able to cause the immunotoxin to bind to said patient's cell;
 - (ii) the second part including a translocation domain of a protein, which domain is capable of translocating the third part across the cytoplasmic membrane of the cell, and
 - (iii) the third part including a polypeptide with the toxic activity of the catalytic domain of toxin LT from Clostridium sordellii LT.
- 9. An immunotoxin according to claim 8, characterized in that the target cell specific binding domain is an antibody or an active fragment thereof.
- 10. Method of manufacturing a therapeutic agent, characterized by combining a therapeutically useful amount of an immunotoxin according to claim 8 with a therapeutically acceptable adjuvant or carrier.

Method of treating a patient with a disorder, characterized by an activating mutation in the Ras proto-oncogene, comprising contacting cells of said patient with a retroviral or non-viral vector utilizable for transformation of tumor cells, which mediates expression of the aminoterminal 1020 amino acids, or a fragment thereof with preserved glucosyltransferase activity.

Vgg/s/